Amendments to Specification

Please amend the specification as follows:

Paragraph at page 3, lines 1-3:

In a fourth embodiment, this invention concerns an isolated polynucleotide encoding an aspartic semialdehyde dehydrogenase, a diaminopimelate decarboxylase, a homoserine kinase, a cysteine synthase~~cysteine γ synthase~~ or a cystathionine β-lyase.

Paragraph at page 4, lines 10-12:

In a thirteenth embodiment, this invention concerns an isolated polypeptide having aspartic semialdehyde dehydrogenase, diaminopimelate decarboxylase, homoserine kinase, cysteine synthase~~cysteine γ synthase~~, or cystathionine β-lyase function.

Paragraph at page 4, lines 17-30:

A further embodiment of the instant invention is a method for evaluating a compound for its ability to inhibit the activity of a plant biosynthetic enzyme selected from the group consisting of aspartic semialdehyde dehydrogenase, diaminopimelate decarboxylase, homoserine kinase, cysteine synthase~~cysteine γ synthase~~ and cystathionine β-lyase, the method comprising the steps of: (a) transforming a host cell with a chimeric gene comprising a nucleic acid fragment encoding a plant biosynthetic enzyme selected from the group consisting of aspartic semialdehyde dehydrogenase, diaminopimelate decarboxylase, homoserine kinase, cysteine synthase and cystathionine β-lyase, operably linked to regulatory sequences; (b) growing the transformed host cell under conditions that are suitable for expression of the chimeric gene wherein expression of the chimeric gene results in production of the biosynthetic enzyme in the transformed host cell; (c) optionally purifying the biosynthetic enzyme expressed by the transformed host cell; (d) treating the biosynthetic enzyme with a compound to be tested; and (e) comparing the activity of the biosynthetic enzyme that has been treated with a test compound to the activity of an untreated biosynthetic enzyme.

Paragraph at page 5, lines 6-12:

Figures 2 through 6 show the amino acid sequence alignments between the known art sequences for aspartic semialdehyde dehydrogenase, diaminopimelate decarboxylase, homoserine kinase, cysteine synthase~~cysteine γ synthase~~, and

cystathione β-lyase with the sequences included in this application. Alignments were performed using the Clustal alogarithm described in Higgins and Sharp (1989) (CABIOS 5:151-153). Amino acids conserved among all sequences are indicated by an asterisk (*) above the alignment. Dashes are used by the program to maximize the alignment. A description of Figures 2 through 6 follows:

Paragraph at page 5, lines 13-23:

Figures 2A, 2B, 2C and 2D show~~Figure 2 shows~~ a comparison of the aspartic semialdehyde dehydrogenase amino acid sequences from corn contig assembled from clones p0003.cgpha22r:fis, cpe1c.pk009.b24, p0016.ctscp83r, and p0075.cslab16r (SEQ ID NO:43), rice clone rlr48.pk0003.d12 (SEQ ID NO:2), the contig of 5' RACE PCR and rice clone rlr48.pk0003.d12 (SEQ ID NO:45), soybean clones sfl1.pk0122.f9 (SEQ ID NO:6), ses9c.pk001.a15:fis (SEQ ID NO:47), and sfl1.pk0122.f9:fis (SEQ ID NO;49), wheat clones wr1.pk0004.c11 (SEQ ID NO:4) and wdk1c.pk014.n5:fis (SEQ ID NO:51) with the *Legionella pneumophila* (NCBI General Identifier No. 2645882; SEQ ID NO:7) and the *Aquifex aeolicus* sequences (NCBI General Identifier No. 6225258; SEQ ID NO:52). Figure 2A: positions 1 through 120; Figure 2B: positions 121 through 240; Figure 2C: positions 241 through 360; Figure 2D: positions 361 through 392.

Paragraph at page 5, lines 24-33:

Figures 3A, 3B, 3C, 3D and 3E show~~Figure 3 shows~~ a comparison of the diaminopimelate decarboxylase amino acid sequences derived from corn clones cen3n.pk0067.a3 (SEQ ID NO:9) and cr1n.pk0103.d8 (SEQ ID NO:11), rice clone rl0n.pk0013.b9 (SEQ ID NO:13), soybean clones sr1.pk0132.c1 (SEQ ID NO:15), sdp3c.pk001.o15 (SEQ ID NO:19) and sdp3c.pk001.o15:fis (SEQ ID NO:54), wheat clones wlk1.pk0012.c2 (SEQ ID NO:17) and wlk1.pk0012.c2:fis (SEQ ID NO:56) with the *Pseudomonas aeruginosa* (NCBI General Identifier No. 118304; SEQ ID NO:20) and *Arabidopsis thaliana* sequences (NCBI General Identifier No. 9279586; SEQ ID NO:57). Figure 3A: positions 1 through 120; Figure 3B: positions 121 through 240; Figure 3C: positions 241 through 360; Figure 3D: positions 361 through 480; Figure 3E: positions 481 through 535.

Paragraph at page 5, line 34 through page 6, line 3:

Figures 4A, 4B and 4C show~~Figure 4 shows~~ a comparison of the homoserine kinase amino acid sequences derived from corn clone cr1n.pk0009.g4 (SEQ ID NO:22), rice clones rca1c.pk005.k3 (SEQ ID NO:24) and rca1c.pk005.k3:fis (SEQ ID NO:59), soybean clone ses8w.pk0020.b5 (SEQ ID NO:26), wheat clone

wl1n.pk0065.f2 (SEQ ID NO:28) with the *Methanococcus jannaschii* (NCBI General Identifier No. 1591748; SEQ ID NO:29) and the *Arabidopsis thaliana* sequences (NCBI General Identifier No. 4927412; SEQ ID NO:60). Figure 4A: positions 1 through 180; Figure 4B: positions 181 though 360; Figure 4C: positions 361 through 396.

Paragraph at page 6, lines 4-12:

Figures 5A, 5B and 5C show~~Figure 5 shows~~ a comparison of the cysteine synthase~~cysteine γ synthase~~ amino acid sequences derived from the corn contig assembled from clones cco1n.pk083.j4, chp2.pk0016.b1, cpd1c.pk004.b20, cr1n.pk0083.c5, csi1.pk0003.g6, and p0126.cnlcb49r (SEQ ID NO:62), rice clone rls6.pk0068.b7:fis (SEQ ID NO:64), soybean clone se3.05h06 (SEQ ID NO:31) with the *Citrullus lanatus* sequence (NCBI General Identifier No. 540497; SEQ ID NO:32), the *Spinacia oleracea* sequence (NCBI General Identifier No. 416869 ~~540497~~; SEQ ID NO:65), and the *Solanum tuberosum* sequence (NCBI General Identifier No. 11131628; SEQ ID NO:66). Figure 5A: positions~~postions~~ 1 through 180; Figure 5B: postions 181 through 360; Figure 5C: positions 361 through 424.

Paragraph at page 6, lines 13-21:

Figures 6A, 6B, 6C and 6D show~~Figure 6 shows~~ a comparison of the amino acid sequences of the cystathionine β-lyase derived from corn clone cen1.pk0061.d4 (SEQ ID NO:34), corn contig assembled from clones p0005.cbmei71r, p0014.ctuui39r, p0109.cdadg47r, and p0125.czaay16r (SEQ ID NO:68), rice clone rlr12.pk0026.g1 (SEQ ID NO:36), the contig of 5' PCR and rice clone rlr12.pk0026.g1:fis (SEQ ID NO:70), soybean clone sfl1.pk0012.c4 (SEQ ID NO:38), and wheat clones wr1.pk0091.g6 (SEQ ID NO:40) and wr1.pk0091.g6:fis (SEQ ID NO:72) with the *Arabidopsis thaliana* sequence (NCBI General Identifier No. 1708993; SEQ ID NO:41). Figure 6A: positions 1 through 120; Figure 6B: positions 121 through 240; Figure 6C: postions 241 through 360; Figure 6D: positions 361 through 483.

Table 1, appearing on pages 7-8:

TABLE 1

Plant Biosynthetic Enzymes

Polypeptide	Clone	SEQ ID NO: (Nucleotide)	(Amino Acid)
rice ASADH	rlr48.pk0003.d12	1	2
wheat ASADH	wr1.pk0004.c11	3	4

soybean ASADH	sfl1.pk0122.f9	5	6
L. pneumophila ASADH	NCBI GI 2645882		7
corn DAPEP	cen3n.pk0067.a3	8	9
corn DAPEP	cr1n.pk0103.d8	10	11
rice DAPEP	rl0n.pk0013.b9	12	13
soybean DAPEP	sr1.pk0132.c1	14	15
wheat DAPEP	wlk1.pk0012.c2	16	17
soybean DAPEP	sdp3c.pk001.o15	18	19
P. aeruginosa DAPEP	NCBI GI 118304		20
corn HK	cr1n.pk0009.g4	21	22
rice HK	rca1c.pk005.k3	23	24
soybean HK	ses8w.pk0020.b5	25	26
wheat HK	wl1n.pk0065.f2	27	28
M. jannaschii HK	NCBI GI 1591748		29
~~soybean CγS~~ soybean CS	se3.05h06	30	31
~~*C. lanatus* CγS~~ *C. lanatus* CS	NCBI GI 540497		32
corn CβL	cen1.pk0061.d4	33	34
rice CβL	rlr12.pk0026.g1	35	36
soybean CβL	sfl1.pk0012.c4	37	38
wheat CβL	wr1.pk0091.g6	39	40
A. thaliana CβL	NCBI GI 1708993		41
corn ASADH	Contig of: p0003.cgpha22r:fis cpe1c.pk009.b24 p0016.ctscp83r p0075.cslab16r	42	43
rice ASADH	5' RACE PCR+ rlr48.pk0003.d12	44	45
soybean ASADH	ses9c.pk001.a15:fis	46	47
soybean ASADH	sfl1.pk0122.f9:fis	48	49
wheat ASADH	wdk1c.pk014.n5:fis	50	51
A. aeolicus ASADH	NCBI GI 6225258		52
soybean DAPEP	sdp3c.pk001.o15:fis	53	54
wheat DAPEP	wlk1.pk0012.c2:fis	55	56
A. thaliana DAPEP	NCBI GI 9279586		57
rice HK	rca1c.pk005.k3:fis	58	59
A. thaliana HK	NCBI GI 4927412		60
~~corn CγS~~ corn CS	Contig of: cco1n.pk083.j4 chp2.pk0016.b1	61	62

	cpd1c.pk004.b20 cr1n.pk0083.c5 csi1.pk0003.g6 p0126.cnlcb49r		
~~rice CγS~~ rice CS	rls6.pk0068.b7:fis	63	64
~~*S. oleracea CγS*~~ *S. oleracea* CS	NCBI GI 416869		65
~~*S. tuberosum CγS*~~ *S. tuberosum* CS	NCBI GI 11131628		66
corn CβL	Contig of: p0005.cbmei71r p0014.ctúui39r p0109.cdadg47r p0125.czaay16r	67	68
rice CβL	5'RACE PCR + rlr12.pk0026.g1:fis	69	70
wheat CβL	wr1.pk0091.g6:fis	71	72

Paragraph at page 10, line 26 through page 11, line 20:

For example, it is well known in the art that antisense suppression and co-suppression of gene expression may be accomplished using nucleic acid fragments representing less than the entire coding region of a gene, and by using nucleic acid fragments that do not share 100% sequence identity with the gene to be suppressed. Moreover, alterations in a nucleic acid fragment which result in the production of a chemically equivalent amino acid at a given site, but do not affect the functional properties of the encoded polypeptide, are well known in the art. Thus, a codon for the amino acid alanine, a hydrophobic amino acid, may be substituted by a codon encoding another less hydrophobic residue, such as glycine, or a more hydrophobic residue, such as valine, leucine, or isoleucine. Similarly, changes which result in substitution of one negatively charged residue for another, such as aspartic acid for glutamic acid, or one positively charged residue for another, such as lysine for arginine, can also be expected to produce a functionally equivalent product. Nucleotide changes which result in alteration of the N-terminal and C-terminal portions of the polypeptide molecule would also not be expected to alter the activity of the polypeptide. Each of the proposed modifications is well within the routine skill in the art, as is determination of retention of biological activity of the encoded products. Consequently, an isolated polynucleotide comprising a nucleotide sequence of at least 30 (preferably at least 40, most preferably at least 60) contiguous nucleotides derived from a nucleotide sequence selected from the group consisting of SEQ ID NOs:1, 3, 5, 42, 44, 46, 48, 50, SEQ ID NOs:8, 10, 12, 14, 16, 18, 53 and 55, SEQ ID NOs:21, 23, 25, 27, and 58, SEQ ID NOs:30, 61, and 63, and SEQ ID NOs:33, 35, 37, 39, 67, 69, and 71 and the complement of such nucleotide

sequences may be used in methods of selecting an isolated polynucleotide that affects the expression of an aspartic-semialdehyde dehydrogenase, a diaminopimelate decarboxylase, a homoserine kinase, a cysteine synthase~~cysteine γ synthase~~, or a cystathionine β-lyase polypeptide in a host cell. A method of selecting an isolated polynucleotide that affects the level of expression of a polypeptide in a host cell may comprise the steps of: constructing an isolated polynucleotide of the present invention or an isolated chimeric gene of the present invention; introducing the isolated polynucleotide or the isolated chimeric gene into a host cell; measuring the level of a polypeptide or enzyme activity in the host cell containing the isolated polynucleotide; and comparing the level of a polypeptide or enzyme activity in the host cell containing the isolated polynucleotide with the level of a polypeptide or enzyme activity in a host cell that does not contain the isolated polynucleotide.

Paragraph at page 18, lines 11-24:

For example, genes encoding other aspartic semialdehyde dehydrogenases, diaminopimelate decarboxylases, homoserine kinases, cysteine synthases~~cysteine γ synthases~~ or cystathionine β-lyases, either as cDNAs or genomic DNAs, could be isolated directly by using all or a portion of the instant nucleic acid fragments as DNA hybridization probes to screen libraries from any desired plant employing methodology well known to those skilled in the art. Specific oligonucleotide probes based upon the instant nucleic acid sequences can be designed and synthesized by methods known in the art (Maniatis). Moreover, an entire sequence can be used directly to synthesize DNA probes by methods known to the skilled artisan such as random primer DNA labeling, nick translation, end-labeling techniques, or RNA probes using available *in vitro* transcription systems. In addition, specific primers can be designed and used to amplify a part or all of the instant sequences. The resulting amplification products can be labeled directly during amplification reactions or labeled after amplification reactions, and used as probes to isolate full length cDNA or genomic fragments under conditions of appropriate stringency.

Paragraph at page 19, line 35 through page 20, line 14:

As was noted above, the nucleic acid fragments of the instant invention may be used to create transgenic plants in which the disclosed polypeptides are present at higher or lower levels than normal or in cell types or developmental stages in which they are not normally found. This would have the effect of altering the level of free amino acids in those cells. Specifically, the enzymes of the present invention form part of the pathway towards the biosynthesis of lysine, threonine, methionine, cysteine and isoleucine. In particular, altering the level and/or function of

cystathionine beta-lyase will result in changes in the rate of methionine biosynthesis. Altering the level and/or function of diaminopimelate decarboxylase will result in changes in the rate of lysine biosynthesis. Altering the level and/or function of aspartate-semialdehyde dehydrogenase will result in changes in the lysine, methionine, or threonine content, especially in wheat. Altering the level of cysteine synthase~~cysteine γ synthase~~ will result in changes in the rate of cysteine and/or methionine biosynthesis; using this gene it will also be possible to control sulfur metabolism. Altering the level of homoserine kinase may be used to regulate threonine and methionine levels. Polypeptides encoding at least a portion of aspartic semialdehyde dehydrogenase, diaminopimelate decarboxylase, homoserine kinase, cysteine synthase, or cystathionine β-lyase may also be used in herbicide identification and design.

Paragraph at page 29, lines 13-20:

Figures 2A, 2B, 2C and 2D show~~Figure 2 shows~~ Figure 2 presents an alignment of the amino acid sequences set forth in SEQ ID NOs:2, 4, 6, 43, 45, 47, 49, and 51 with the *Legionella pneumophila* sequence (NCBI General Identifier No. 2645882; SEQ ID NO:7) and the *Aquifex aeolicus* sequence (NCBI General Identifier No. 6225258; SEQ ID NO:52). The data in Table 5 presents a calculation of the percent identity of the amino acid sequences set forth in SEQ ID NOs:2, 4, 6, 43, 45, 47, 49, and 51 with the *Legionella pneumophila* sequence (NCBI General Identifier No. 2645882; SEQ ID NO:7) and the *Aquifex aeolicus* sequence (NCBI General Identifier No. 6225258; SEQ ID NO:52).

Paragraph at page 32, lines 5-12:

Figures 3A, 3B, 3C, 3D and 3E present~~Figure 3 presents~~ an alignment of the amino acid sequences set forth in SEQ ID NOs:9, 11, 13, 15, 17, 19, 54, and 56 with the *Pseudomonas aeruginosa* sequence (NCBI General Identifier No. 118304; SEQ ID NO:20) and the *Arabidopsis thaliana* sequence (NCBI General Identifier No. 9279586, SEQ ID NO:57). The data in Table 8 presents a calculation of the percent identity of the amino acid sequences set forth in SEQ ID NOs:9, 11, 13, 15, 17, 19, 54, and 56 with the *Pseudomonas aeruginosa* sequence (NCBI General Identifier No. 118304; SEQ ID NO:20) and the *Arabidopsis thaliana* sequence (NCBI General Identifier No. 9279586; SEQ ID NO:57).

Paragraph at page 34, lines 1-8:

Figures 4A, 4B and 4C present~~Figure 4 presents~~ an alignment of the amino acid sequences set forth in SEQ ID NOs:22, 24, 26, 28, and 59 with the

Methanococcus jannaschii sequence (NCBI General Identifier No. 1591748; SEQ ID NO:29) and the *Arabidopsis thaliana* sequence (NCBI General Identifier No. 4927412; SEQ ID NO:60). The data in Table 11 presents a calculation of the percent identity of the amino acid sequences set forth in SEQ ID NOs:22, 24, 26, 28, and 59 with the *Methanococcus jannaschii* sequence (NCBI General Identifier No. 1591748; SEQ ID NO:29) and the *Arabidopsis thaliana* sequence (NCBI General Identifier No. 4927412; SEQ ID NO:60).

Title for Table 12 at page 35, lines 3-4:

BLAST Results for Sequences Encoding Polypeptides Homologous to Cysteine Synthase~~Cysteine γ Synthase~~

Paragraph at page 35, lines 6-13:

Further sequencing and searching of the DuPont proprietary database allowed the identification of corn and rice clones encoding polypeptides with similarities~~similarites~~ to cysteine synthase~~cysteine γ synthase~~. The BLAST search using the sequences from clones listed in Table 13 revealed similarity of the polypeptides encoded by the cDNAs to cysteine synthase~~cysteine γ synthase~~ from *Spinacia oleracea* (NCBI General Identifier No. 416869) and *Solanum tuberosum* (NCBI General Identifier No. 11131628). Shown in Table 13 are the BLAST results for the sequences of the entire cDNA inserts comprising the indicated cDNA clones encoding the entire protein ("CGS"):

Title for Table 13 at page 35, lines 16-17:

BLAST Results for Sequences Encoding Polypeptides Homologous to Cysteine Synthase~~Cysteine γ Synthase~~

Paragraph at page 35, lines 19-27:

Figures 5A, 5B and 5C present~~Figure 5 presents~~ an alignment of the amino acid sequences set forth in SEQ ID NOs:31, 62, and 64 with the *Citrullus lanatus* sequence (NCBI General Identifier No. 540497; SEQ ID NO:32), *Spinacia oleracea* (NCBI General Identifier No. 416869; SEQ ID NO:65), and the *Solanum tuberosum* sequence (NCBI General Identifier No. 11131628; SEQ ID NO:66). The data in Table 14 presents a calculation of the percent identity of the amino acid sequences set forth in SEQ ID NOs:31, 62, and 64 with the *Citrullus lanatus* sequence (NCBI General Identifier No. 540497; SEQ ID NO:32), *Spinacia oleracea* (NCBI General Identifier No. 416869; SEQ ID NO:65), and the *Solanum tuberosum* sequence (NCBI General Identifier No. 11131628; SEQ ID NO:66).

Title for Table 14 at page 36, lines 2-4:

Percent Identity of Amino Acid Sequences Deduced From the Nucleotide Sequences of cDNA Clones Encoding Polypeptides Homologous to Cysteine Synthase~~Cysteine γ Synthase~~

Paragraph at page 36, lines 6-15:

Sequence alignments and percent identity calculations were performed using the Megalign program of the LASERGENE bioinformatics computing suite (DNASTAR Inc., Madison, WI). Multiple alignment of the sequences was performed using the Clustal method of alignment (Higgins and Sharp (1989) *CABIOS.* *5*:151-153) with the default parameters (GAP PENALTY=10, GAP LENGTH PENALTY=10). Default parameters for pairwise alignments using the Clustal method were KTUPLE 1, GAP PENALTY=3, WINDOW=5 and DIAGONALS SAVED=5. Sequence alignments and BLAST scores and probabilities indicate that the nucleic acid fragments comprising the instant cDNA clones encode entire corn, rice, and soybean cysteine synthases~~cysteine γ synthases~~. These sequences represent the first corn, rice, and soybean sequences encoding cysteine synthase~~cysteine γ synthase~~ known to Applicant.

Paragraph at page 37, line 22 through page 38, line 3:

Figures 6A, 6B, 6C and 6D present~~Figure 6 presents~~ an alignment of the amino acid sequences set forth in SEQ ID NOs:34, 36, 38, 40, 68, 70, and 72 with the *Arabidopsis thaliana* sequence (NCBI General Identifier No. 1708993; SEQ ID NO:41). The data in Table 17 presents a calculation of the percent identity of the amino acid sequences set forth in SEQ ID NOs:34, 36, 38, 40, 68, 70, and 72 with the *Arabidopsis thaliana* sequence (NCBI General Identifier No. 1708993; SEQ ID NO:41).